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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/707,892	11/06/2000	Robert H. Austin	4555-107 US	9832

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EXAMINER	
BROWN, JENNINE M	
ART UNIT	**PAPER NUMBER**
1755	

18

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/707,892	AUSTIN ET AL.
	Examiner	Art Unit
	Jennine M. Brown	1755

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/04/2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

Examiner has entered Applicants amendment, which obviates Examiners previous rejections, therefore these rejections have been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 10, 13, 15-18, 21 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063).

Regnier, et al. teach a microfluidic device with a plurality of constrictions (14) separated from one another by a gap (12, 104) and a means for passing polarizable particles in the vicinity of the constrictions by applying a dielectrophoretic field (Figure 4A) to trap particles in the gap (Figures 1A-8; col. 2, l. 1-62; col. 4, l. 61 – col. 5, l. 7; col. 5, l. 37-55; col. 12, l. 53 – col. 16, l. 65). Regnier, et al. teach a fluid input means for inputting fluid (col. 2, l. 29-35).

Regnier, et al. teach an electrical signal applied to a pair of electrodes on opposite edges of substrate (col. 9, l. 61-67). Regnier, et al. teach that the constrictions are formed on a substrate using a photolithographic etch (abstract; col. 4, l. 26 – col. 5, l. 36). Regnier, et al. teach that the distance between constrictions is not to exceed 10 to 100 micrometers (col. 4, l. 5-10; col. 7, l. 21-23). Regnier et al. teach a distance between rows of constrictions having varied geometric shapes and those rows can be equally spaced or differently spaced as shown in Figures 1A-6. Regnier, et al teach that the substrate can be quartz and silicon (col. 4, l. 49-51). Regnier, et al. teach that there is a cover plate (13) used which is sealed to the substrate (col. 5, l. 8-23). Regnier, et al. teach through Figure 1A an area of tightly placed constrictions (top of drawing) next to fewer more widely spaced constrictions (branches towards middle of drawing) to even further spaced apart constrictions (branches towards bottom left hand side of drawing). Regnier, et al. do not teach a dielectric force. Becker, et al. provides evidence that both electrophoretic and dielectrophoretic forces can be obtained by using the same type of apparatus (col. 5, l. 31-33). Becker, et al. teach an electrophoretic apparatus made of glass, silicon dioxide, polymer, ceramic or any suitable electrically insulating material (col. 12, l. 33-41) having inlets and outlets where syringe needle, micropipette, tube or any other suitable device are used to introduce polarizable particles (col. 12, l. 47-49; col. 12, l. 66 – col. 12, l. 1) where the apparatus has electrode arrays controlled by a computer where electrodes can be in two dimensional groupings of columns and rows such that the surface gives an interaction site for the polarizable particles to interact (col. 3, l. 56-67) using electrodes in the array that are individually programmable and addressable by a controller (col. 4, l. 39-46) where the spacing of the electrodes is between 1 micron and 200 microns (col. 5, l. 1-3) and the force used is an inhomogeneous electrical field which is either AC or DC (col. 8, l. 31-47; col. 13, l. 37-49) and

can be switched by the controller (col. 13, l. 62 – col. 14, l. 5) whereby the frequency can be generated up to GHz and more particularly between 1 kHz and 10 MHz (col. 17, l. 9-14). Becker, et al. also teach that hydrophobic coatings can be used on the reaction surface (col. 4, l. 16-18) and that the polarizable particles can be moved, fused, merged, mixed, reacted, metered, divided, split, sensed, collected or any combination thereof. The sensing equipment used is either electrical or CCD camera (23; col. 8, l. 14-16).

It would have been obvious to one of ordinary skill in the art to modify the apparatus of Regnier, et al. to use the programmable electrode array of Becker, et al. and the sensing methods of Becker, et al. to trap polarizable particles at the constrictions because one can programmably manipulate the polarizable particles for different biochemical protocols such as metering, mixing, transporting, division, or other manipulation of fluids so that reagents, intermediates and or final reaction products can be monitored, measured or sensed in parallel or serially in an analytical apparatus to quantitate results, saving time and money.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Kopf-Sill, et al. (US 6358387).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above but do not specifically teach the heating means adjacent said constrictions. Kopf-Sill, et al. teach the use of heating means adjacent to the channels in a microfluidic chip which uses electrofocusing of analytes (col. 9, l. 36 – col. 10, l. 20).

It would have been obvious to one of ordinary skill in the art to add the heating block layer element of Kopf-Sill, et al. to the apparatus of Regnier, et al. in view of Becker, et al.

because it would aid in heating or cooling of separated materials for further denaturing, chelating or other reactions where heating or cooling is required so that labeling agents or taggants can be added to a biochemical analyte in order to detect fluorescence in the material.

Claims 5-7, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Walters, et al. (US 6117660).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regarding claims 5-7, Regnier, et al. in view of Becker, et al. specifically teach AC voltages at a predetermined frequency or DC voltage as described previously. Walters, et al. also teach AC or DC voltages at a predetermined frequency for dielectrophoresis (col. 1, l. 49-52) specifically the range of 1Hz (col. 2, l. 39-48; col. 3, l. 23-24; col. 4, l. 7-10, 44-48; col. 5, l. 64-65; col. 6, l. 15-16, 26-28, 34-35; col. 7, l. 13-16, 19-21; col. 10, l. 27-37).

It would have been obvious to one of ordinary skill in the art to use the predetermined AC voltage frequency of Walters, et al. in the apparatus of Regnier, et al. in view of Becker, et al. because it will provide for dielectric pumping of analyte in an electrophoretic apparatus where low temperatures are required and where the coating on the monolithic structures acts similarly to a treated membrane which is used in the electroportation and electrofusion art.

Regarding claim 9, Regnier, et al. in view of Becker, et al. teach using coating moieties of anionic groups, cationic groups, antibodies, antigens and chelation groups which are used to bind things like ssDNA, dsDNA, RNA, cells and polymer particles but do not specifically address biological polymers as the particles being separated. Walters, et al. teach that apparatus for electromanipulation (i.e. electrophoresis) is used on DNA material (col. 2, l. 67), cell

membranes (col. 2, l. 6-7) and other materials as discussed in the background of the art (col. 1, l. 13 - col. 10, l. 37). It would have been obvious to one having ordinary skill in the art to specifically separate biological polymers with the device of Regnier, et al. in view of Becker, et al. because biological polymers are specifically responsive to electrophoresis and dielectrophoresis.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Austin, et al. (US 5427663).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regarding claim 11, Regnier, et al. in view of Becker, et al. do not specifically teach the height between 0.5 to 5 micrometers. Austin, et al. teach a microfluidic device with the same types of constrictions used by Regnier, et al. in view of Becker, et al. where the height range is between 0.01 and 20.0 micrometers.

It would have been obvious to one of ordinary skill in the art to modify the apparatus of Regnier, et al. in view of Becker, et al. to decrease the height of the apparatus as is stated by Austin, et al. so that the obstacles had a height between 0.01 and 20.0 micrometers because this would constrict the separating mixture to one layer of cells, particles or other analyte to be separated.

Regarding claim 12, Regnier, et al. in view of Becker, et al. state that the preferred distance between the constrictions is 1 micrometer and it would have been obvious to one of ordinary skill in the art to using the reasoning stated regarding claim 11 that the height would

need to be large enough to reduce the amount of Joule heating while being small enough to allow only particles of analytes like RNA and DNA to be separated out.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Austin, et al. (US 5427663) or Christel, et al. (US 6368871).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regnier, et al. in view of Becker, et al. do not specifically teach a trapezoidal shape for the constrictions, but it would have been obvious for one of ordinary skill in the art to change the shape of the constriction. Austin, et al. also teach different shapes for constrictions (col. 20, l. 41-44) although trapezoidal shaped is not specifically shown, the arrow shaped constrictions shown in Figure 7 resemble a trapezoidal shape enough that it would have been obvious to one of ordinary skill in the art to substitute a shape change for the constriction because it can easily be changed during the lithography of the substrate. Figures 1b, 1c, 1d and 1f of Christel, et al. show different shapes including trapezoidal (1F). Also the Applicants disclosure does not state any specific advantage that the trapezoidal shape gives over all shapes shown for the configurations and it appears taht the invention would perform equally well using the constriction shapes taught by Regnier, et al., Austin, et al. or Christel, et al. and would have been obvious to one of ordinary skill in the art to use different shaped constrictions, because it would merely be a matter of design choice.

Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Quake, et al. (US 6344325).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regarding claim 19, Regnier, et al. in view of Becker, et al. do not specifically teach one or more channels coupled to the end of the regions for extracting polarizable particles. Quake, et al. teach a microfluidic device having one or more channels coupled to the end of regions for extracting polarizable particles (Figures 1-7; col. 2, l. 39 -56).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. in view of Becker, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions.

Regarding claim 20, Regnier, et al. in view of Becker, et al. do not specifically teach a matrix in a channel downstream from the constrictions capable of fractioning and/or analyzing the particles. Quake, et al. teach fractioning and analyzing the particles separated (col. 2, l. 57 – col. 5, l. 46).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. in view of Becker, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions because each constriction would be identified by another means such as fluorescent imaging.

Regarding claim 22, Regnier, et al. in view of Becker, et al. teach siloxane substrates as explained previously but do not specifically teach substrate material of polyimide, PDMS or

PMMA. Quake, et al. teach PMMA as a substrate resist material deposited on the surface of the substrate.

It would have been obvious to one of ordinary skill in the art to use PMMA photoresist as the etchant material for the substrate because it would have the hydrophobicity required for certain types of wall materials created for the channels of the substrate and is easier to control and cheaper to use than traditional wet etching methods.

Response to Arguments

Applicant's arguments filed on 08/04/2003 have been fully considered but they are not persuasive.

Examiner incorporates the teachings of the article written by Michael Hughes "AC Electrokinetics: Applications for Nanotechnology" that was published 30 November 1999 online at http://www.foresight.org/Conferences/MNT7/Papers/Hughes/index.html as evidence that the apparatus of Regnier, et al. may be used for trapping as well as separating particles. Hughes teaches that dielectrophoretic forces may be viewed as an electrostatic equivalent to optical tweezers (page 2, first pgh) and that trapping of particles using microelectronic devices using these forces are known (page 2, second pgh). Two sets of stacked electrodes were envisioned for manipulation of a particle in a field to act like a cage (page 7, first pgh) and an alternate approach would be to use an AFM tip to provide this manipulation (page 9, first pgh).

Becker, et al. (US 6294063) was used by Examiner in evidence that both electrophoretic and dielectrophoretic forces can be used to move materials using the same apparatus and it can be used for trapping polarizable particles in the vicinity of the substrate as evidenced in the specification of Becker, et al. supra.

Regnier, et al. teach the use of electrodes which are used to exert potential. An electrode can be used to generate either AC or DC potential depending on the controller that is used. It was previously determined by the Becker, et al. reference that there is an equivalence between AC and DC forces because both electrophoretic (primarily DC) and dielectrophoretic (primarily AC) forces can be used in the apparatus. Figures 4A and 4B (Regnier, et al.) show a voltage difference between the obstacles, therefore trapping can occur between these structures when AC is used. Examiner retracts the statement that prior art does not describe or suggest the use of a material having a dielectric constant less than the buffer where the particles to be trapped are suspended to provide a material that the field lines cannot penetrate. Examiner points out that the constrictions of Regnier, et al. (col. 4, l. 50-51) are made of the same materials as those disclosed by Applicants (spec. p. 8, l. 3-6; e.g., glass, quartz, PMMA) and therefore the electric field lines can not penetrate the constrictions and can isolate the particles where the constrictions are smallest. The walls of the constrictions do not necessarily need to be coated but one of the preferred embodiments envisions a coating on the constriction so that it may more easily trap particular types of materials such as an antigens or antibodies.

Kopf-Sill was used to cure a deficiency regarding heating/cooling means for the constrictions not the flow path or trapping means.

Walters teaches the pulse field generator used in wells similar to those of the primary reference, which can be "crated in DC or AC fields" (col. 1, l. 50) and is used to show that multiple wells can be manipulated with an electrical field which can be the same or different depending on the ability of the controller.

Austin was used to show that the constrictions can be made in any shape, width or depth desired using microlithographic techniques and that it would not be novel to change the shape of the constrictions.

In regard to the Quake, et al. reference, Examiner reminds Applicants that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Applicants admit that the apparatus of Quake, et al. is similar to that of Regnier, et al. because they both teach microchannel arrangement whereby the constrictions taught by Regnier, et al. can be added into a modified microchannel arrangement of Quake, et al. to suggest Applicants apparatus.

Allowable Subject Matter

The indicated allowability of claim 34 is withdrawn in view of the definition of the materials that the constrictions are comprised of.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennine M. Brown whose telephone number is (703) 305-0435. The examiner can normally be reached on M-F 8:00 AM - 6:00 PM; first Friday off.

After the move to the new USPTO Headquarters in Alexandria, VA, tentatively scheduled for the week of December 22, 2003, the examiner's new phone number will be (571) 272-1364 and Mr. Bell's new phone number will be (571) 272-1362.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Bell can be reached on (703) 308-3823. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

jmb

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